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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,746	06/06/2005	Leonardo De Maria	10319.204-US	5078

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EXAMINER	
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ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,746	DE MARIA ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-43* is/are pending in the application.

4a) Of the above claim(s) *42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 29-43 are currently pending.

This application is a 371 of PCT/DK2003/000851.

The preliminary amendment filed on 11/29/2007, canceling claims 1-28 and adding new claims 29-43 is acknowledged.

Election/Restriction

Applicant's election with traverse of Group I claims claim(s) 1-2, 6, 10, 14 and 18-21, drawn to a variant of a parent glycoside hydrolase family 53 galactanase, and a variant polypeptide having a mutation at position 90 in the communication filed on 11/29/2007 is acknowledged.

The traversal is on the ground(s) that newly added claims are directed to variants of a parent glycoside hydrolase family 53 galactanase comprising an alteration at least in one of the positions 90, 91, 183, 303, 305 and 313, wherein the variants share a special technical feature. This is not found persuasive because a variant A90S recited in claim 29 is known in the art (UniProt Accession No. Q9Y7F8, created on 11/1/1999). Therefore, a variant of galactanase at position 90 does not make contribution over the prior art and lack unity of invention. Besides the variants polypeptide recited in the claims do not have special technical feature among each other because they all represent structurally different polypeptides and polynucleotide encoding them.

Applicants also argue that IPER did not raise any question about lack of unity at any point during PCT prosecution. This is not found persuasive because the Examiner finds that lack of unity exists as discussed above and examination in the national phase (as 371 Application) is

not bound by the international phase (PCT) findings. Besides examining all the groups and all the variants would impose a serious burden to the Office.

As restriction is clearly permissible even among related inventions as defined in MPEP 808 and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct.

The requirement is still deemed proper and is therefore made **FINAL**.

Newly added Claim 42, directed to an animal feed composition comprising said variant polypeptide is withdrawn from further consideration as reciting a nonelected invention, since claim 42 recite a new invention i.e. an animal feed composition that is a complex composition besides the variant polypeptide which should be grouped as a new Group III and newly added claim 43 recites a method, which should be grouped as a new Group IV. The method of Group IV does not share any special technical feature with Group II, as polynucleotide of Group II is neither made nor used by the methods of Group IV. The method of Group IV is not rejoinable with the variant polypeptide because the claims lack unity of invention as discussed above.

Therefore, claims 42 and 43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 29-41 are under consideration and are present for examination.

Priority

Acknowledgement is made of applicants claim for priority of provisional applications 60/437,615 filed on 1/2/2003 and 60/461,230 filed on 4/8/2003. In addition, acknowledgement is made for foreign priority of applications DENMARK PA 2002/01968 filed on 12/20/2002 and DENMARK PA 2003/00537 filed on 4/8/2003.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 06/06/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is considered by the examiner. The signed copy of IDS is enclosed herewith.

Drawings

There is no drawing with this application.

Specification/Informalities

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 12 and 13). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is requested.

Specification/Informalities

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 121 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

If applicant desires priority under 35 U.S.C. 121 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title,

preferably as separate paragraph. The status of non-provisional parent application(s) (whether patented or abandoned) should also be included. *If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.*

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

Claims 29, 31-32, 34, 36 and 38 are objected to as encompassing non-elected subject matter. Appropriate correction is requested.

Claim 38 is objected to in the recitation of "K-6P", which should be "K6P". Appropriate correction is requested.

Claim 38 is objected to in the recitation of "S-4P", which should be "S4P". Appropriate correction is requested.

Claim 38 is objected to in the recitation of "L-2P", which should be "L2P". Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 29-41 are directed to a variant of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity, wherein the position is the number of corresponding amino acid residue in SEQ ID NO: 1, wherein the parent galactanase is 25% sequence identity to SEQ ID NO: 1.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical*).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.* the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description (see *Enzo* paraphrase above).

Thus, Claims 29-41 are directed to any variant polypeptide of a parent glycoside hydrolase Family 53 galactanase of SEQ ID NO: 1, comprising an alteration at position 90 having galactanase activity, wherein the position is the number of corresponding amino acid residue in SEQ ID NO: 1, wherein the parent galactanase is 25% sequence identity to SEQ ID NO: 1.

Claims are thus drawn to any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase of SEQ ID NO: 1, comprising an alteration at position 90 having galactanase activity, wherein the position is the number of corresponding amino acid residue in SEQ ID NO: 1, wherein said variant polypeptides structures are not fully described in the specification. No information, beyond the characterization of a polypeptide having an alteration at position 90 having galactanase activity, wherein the parent galactanase is 25% sequence identity to SEQ ID NO: 1, which would indicate that applicants had possession of the claimed genus of any variant polypeptide having galactanase activity, the variant has an alteration at position with any amino acids and having 25% sequence identity to SEQ ID NO: 1. The specification does not contain any disclosure of the structure of all the variants of a

polypeptide having galactanase activity as claimed. The genus of variant is a large variable genus including many mutants and variants, which can have wide variety of structures. Therefore, many structurally unrelated polypeptides are encompassed within the scope of the claims. The specification discloses few representative species of parent polypeptides and few variant, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 29-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific variant polypeptides of A90S and H91D derived from SEQ ID NO: 1 of Myceliophthora thermophila and D181N, S90A and D91H derived from SEQ ID NO: 3 of Aspergillus aculeatus, does not reasonably provide enablement for any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity or any variant polypeptide, which is 25% sequence identity to SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, **to make and use** the claimed invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731,737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows:

(1) quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence and absence of working examples, (4) the nature of the invention, (5) the state of prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The factors, which have, lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed below:

The breath of the claims:

Claims 29-41 are so broad as to encompass any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity or any variant polypeptide, which is 25% sequence identity to SEQ ID NO: 1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variant polypeptides broadly encompassed by the claims. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only few variants such as A90S and H91D of SEQ ID NO: 1 and D181N, S90A and D91H of SEQ ID NO: 3.

The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art:

The amino acid sequence of a polypeptide determines its structural and functional properties. While the specification discloses few variants of SEQ ID NO: 1 or SEQ ID NO: 3 having galactanase activity, neither the specification nor the art provide a correlation between structure and function such that one of skill in the art can envision the structure of any variant polypeptide having an alteration at position 90 of SEQ ID NO: 1 or any variant polypeptide

which is 25% identity to SEQ ID NO: 1. The art clearly teaches that modification of a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are tolerant of modification and which ones are conserved is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. (1999) and Seffernick et al. (2001), where it is shown that even small amino acid changes result in enzymatic activity changes.

The quantity of experimentation required practicing the claimed invention based on the teachings of the specification:

While methods of generating variants of a polypeptide were well known in the art at the time of invention, it is not routine in the art to screen by trial and error process for (1) any variant polypeptide of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity, or (2) any variant protein which is 25% identical to SEQ ID NO: 1, (3) an essentially infinite number of variants of a parent glycoside hydrolase Family 53 galactanase protein sequence. The amino acids modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the

result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

The amount of direction or guidance presented and the existence of working examples:

The specification discloses for specific variant polypeptides of A90S and H91D derived from SEQ ID NO: 1 of Myceliophthora thermophila and D181N, S90A and D91H derived from SEQ ID NO: 3 of Aspergillus aculeatus. However, the specification fails to provide any clue as to the structural elements required in any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity or any variant polypeptide, which is 25% sequence identity to SEQ ID NO: 1 or which are the structural elements in said any variant polypeptides known in the art that are essential for successfully practice the claimed invention. No correlation between structure and function has been presented.

The specification does not support the broad scope of the claims which encompass any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity or any variant polypeptide, which is 25% sequence identity to SEQ ID NO: 1 because the specification does **not** establish: (A) regions of the variant protein structure which may be modified without affecting galactanase activity and; (B) the general tolerance of any variant polypeptide of parent glycoside hydrolase Family galactanase to modification and extent of such tolerance; (C) a rational and predictable

scheme for modifying any glycoside hydrolase Family galactanase amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art **to make and use** the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase or any variant polypeptide which is 25% identity to SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any variant polypeptide having any structure of a parent glycoside hydrolase Family 53 galactanase, or any variant polypeptide, which is 25% sequence identity to SEQ ID NO: 1 having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29-35, and 38-41 are rejected under 35 U.S.C. 102(b) as being anticipated by UniProt Accession No. Q9Y7F8, created 11/1/1999, see sequence alignment). Claims are directed to any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity or any variant polypeptide, which is 25% sequence identity to SEQ ID NO: 1.

Q9Y7F8 discloses a polypeptide having a mutation at position 90, wherein A90 is substituted with serine (A90S), wherein the polypeptide has arabinogalactan endo-1,4-beta-galactosidase activity, which is the galactanase as claimed (see EC 3.2.1.89) that is isolated from an Aspergillus species. Q9Y7F8 also discloses that said polypeptide also comprises a mutation at position 91 H91D (for claim 32), which is 63% identical to SEQ ID NO: 1 (for claim 40) that is derived from M. thermophila, which is inherently a variant of a galactanase isolated from M. thermophilus as well as H. insolens or B. licheniformis respectively. Therefore, Q9Y7F8 anticipates claims 29-35, and 38-41 of the instant application.

Claims 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Kofod et al. (US Patent 6329185, publication 12/11/2001, see sequence alignment). Claims are directed to any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity, which is a variant of an Aspergillus aculeatus species.

Kofod et al. disclose a galactanase polypeptide from M. giganteus having a mutation at position 90, wherein the amino acid residue is glycine (G), wherein the polypeptide has galactanase activity. The galactanase protein of Kofod et al. indeed a variant of a galactanase

isolated from Aspergillus aculeatus. Therefore, Kofod et al. anticipate claims 37 and 38 of the instant application.

Conclusion

Status of the claims:

Claims 29-43 are pending.

Claims 42 and 43 are withdrawn.

Claims 29-41 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

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